The role of stem cell source in autologous hematopoietic stem cell transplantation for patients with myelodysplastic syndromes

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Background and Objectives. Intensive chemotherapy followed by autologous hematopoietic stem cell transplantation (HSCT) is a curative treatment option for patients with myelodysplastic syndromes (MDS). Peripheral blood (PB) HSCT was introduced in 1992 and PB has become the source of choice of autologous stem cells worldwide. Autologous PB stem cells result in faster hematopoietic recovery, but may be associated with a higher risk of relapse.

Design and Methods. We analyzed the data of 336 patients transplanted after 1992 with either bone marrow (BM) (n=104) or PB (n=232).

Results. Various factors had an impact on event-free survival in univariate analysis: age (hazard ratio [HR]=1.1 per 10 years; p=0.12), source of stem cells (HR=1.2, p=0.22), interval between diagnosis and transplantation (HR=1.0 per month; p=0.87), and therapy-related vs primary disease (HR=0.5; p=0.002). In the multivariate Cox model, the event-free survival was not different after PB or BM HSCT with a HR of 0.93 (95% confidence interval of 0.67 - 1.30; p=0.67). The relapse risk after transplantation with stem cells from either source was similar with a HR of 1.1. A significant interaction (p=0.02) between age and the source of stem cells indicated a more favorable potential of autologous PB HSCT in young age groups.

Interpretation and Conclusions. Autologous PB and BM HSCT result in equivalent outcomes. Therefore, given the more rapid hematopoietic recovery PB is the preferred source of stem cells.

Key words: autologous hematopoietic stem cell transplantation, myelodysplastic syndromes, secondary acute myeloid leukemia, mobilized peripheral blood stem cells, bone marrow stem cells.

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The natural history of myelodysplastic syndromes (MDS) is variable and depends on the stage of the disease.[1,2] The prognosis of patients with advanced stages of MDS, therapy-related MDS, or secondary acute myeloblastic leukemia (AML) is generally poor with median survivals of less than 12 months. Various classification systems have been used to predict the outcome of MDS patients.[3] For young patients with high-risk MDS allogeneic stem cell transplantation is a curative option. However, an HLA-identical sibling is only available for one-third of patients. Disease-free survival after allogeneic stem cell transplantation ranges between 35-45%.[4-11] Intensive chemotherapy with AML-like schedules followed by autologous stem cell transplantation may provide an alternative option for patients lacking a suitable donor. Intensive chemotherapy results in complete remission rates of 15-65%.[12-16] The median remission duration without stem cell transplantation is usually short due to a high incidence of early relapses. In view of the high relapse rate after chemotherapy alone transplantation with autologous stem cells after remission induction and consolidation chemotherapy has been applied in various clinical studies.[17-19] In 1997 the European Group for Blood and Marrow Transplantation (EBMT) reported the results of 79 patients with MDS, secondary AML or therapy-related AML who received an autograft in first complete remission after chemotherapy. The 2-year survival, disease-free survival and relapse rates were 39%, 34% and 64%, respectively.[18] Autologous bone marrow (BM) stem cells for these indications are associated with prolonged marrow hypoplasia. Therefore, peripheral blood (PB) has rapidly replaced BM as the preferred source of stem cells for autologous hematopoietic stem cell transplantation (HSCT).[20] Early analyses indicated an increased risk of relapse after autologous PB HSCT, particularly in patients over 40 years old.[21]

The Chronic Leukemia Registry of the EBMT contained 432 reports of patients autografted for MDS or secondary leukemia in first complete remission. We wanted to use these data to determine the efficacy of both stem cell sources for autologous stem cell transplantation in these patients, by assessing overall survival, disease-free survival, transplant-related mortality, and relapse risk. In addition, we wanted to study the effects of various prognostic factors, such as stage and nature of disease, transplant year, cytogenetic characteristics, and patients' age, on the outcome of transplants. For these reasons we collected additional information on potential prognostic variables in this setting, such as year of transplant, interval between diagnosis and first complete remission, interval between first complete remission and transplant, age, type of MDS

(therapy-related vs primary MDS or AML-MDS, and cytogenetics. The main purpose of this analysis was to test whether the change to PB as the source of stem cells in this setting has worsened the outcome of HSCT.

Design and Methods

Data were retrieved from the registries of the Chronic and Acute Leukemia Working Parties of the European Group for Blood and Marrow Transplantation. These registries continuously collect data related to patients transplanted by member teams. Reports were available for 432 patients transplanted in first complete remission: 76 with primary MDS, 141 with acute leukemia secondary to MDS and 79 patients with MDS or secondary leukemia after cytotoxic therapy for an unrelated disease. The disease classification was incomplete in 136 patients mainly due a lack of information on prior cytotoxic therapy in 114 patients with MDS. The median age of the 432 patients was 49 years (range: 0-73 years) and 198 (46%) were older than 50 years at the time of transplant. The median interval between diagnosis and transplantation was 6 months (range: 1-42 months) for the 76 patients with MDS and 6 months (range: 1-89 months) for the patients transplanted for secondary AML or therapy-related MDS/AML. Cytogenetic data were available for 136 patients. Patients were stratified according to the International Prognostic Scoring System (IPSS) cytogenetic classification into three risk groups. The source of stem cells was BM only in 155 patients, 234 patients were treated with mobilized PB stem cells and 34 patients received stem cells from both sources. The origin of the stem cells was not completely clear in 7 patients. None of the stem cell grafts was subjected to purging procedures. The analysis of this study was restricted to patients transplanted after 1992 for several reasons: autologous PB HSCT was introduced in 1992, the average age of patients transplanted before 1992 was generally lower, experience and supportive care may be different in the two periods, and finally the outcomes of most patients transplanted before 1992 have already been reported.[18]

Definitions

MDS and AML were classified according to the criteria of the French-American-British (FAB) working group.[2] AML developing after antecedent myelodysplasia lasting at least 3 months is defined as secondary AML (or secondary leukemia). MDS or AML occurring after chemotherapy or radiotherapy is defined as therapy-related MDS or therapy-related AML. Complete remission is defined as a normocellular marrow with less than 5% blast cells including monocytoid cells and <10% blast cells + promyelocytes. Peripheral blood counts should be in the normal range.

Statistical analysis

The time intervals for survival, relapse-free survival, relapse and transplant-related mortality were calculated from the day of stem cell transplantation onwards. For the Kaplan-Meier curves (used in univariate descriptions) and Cox models (used to estimate hazard ratios) the relapsed patients were censored for transplant-related mortality at the time of relapse and *vice versa*. Univariate comparisons of Kaplan-Meier curves were performed using the two-tailed log-rank test. For ordered categorical variables the trend version of the log-rank test was used. The association of various risk factors with the outcomes (overall survival, disease-free survival, relapse incidence and transplant-related mortality) was quantified using the hazard ratios estimated in the Cox models. Actual multivariate estimates for relapse incidence and transplant-related mortality were made using cumulative incidence estimates. The sum of these two cumulative incidences equals the complement of the disease-free survival. Calculations were performed using SPSS version 11. The cumulative incidences were calculated in NCSS version 2001.

All models are full models in the sense that no stepwise backward reduction of models was performed. Interactions of the main risk factor of interest, the source of stem cells, with all other covariates were tested in a stepwise backwards manner. For the sake of simplicity interactions with p-values between 0.05 and 0.10 were removed if the hazard ratios among the strata were pointing in the same direction (i.e. either both indicating an increased or a decreased risk). The analyses were only carried out on cases for which sufficient information was available. This meant that two transplants, which had a relevant missing value, were removed from the analysis. The date of the analysis was September 26, 2005.

Results

Patients' characteristics

The average age of patients at transplantation was higher in more recently performed transplantations. Patients transplanted before 1997 were generally younger with only 43% of the patients older than 50 years while 56% of the patients transplanted after 1996 were older than 50 years. Seventy-four percent of the patients over 60 years old were transplanted after 1996. The average age of patients transplanted with mobilized blood cells was higher than that of patients who received autologous BM (Table 1). Only eight patients treated with autologous BM HSCT (8%) were older than 60 years in contrast to 60 patients (26%) who received autologous PB HSCT. The interval between diagnosis and transplantation did not differ according to the source of stem cells (Table 1). Therapy-related MDS/AML was not more frequently observed in patients transplanted with mobilized blood stem cells. The cytogenetic risk groups were also equally divided between PB and BM HSCT recipients (Table 1).

Univariate analyses using Kaplan-Meier curves and log-rank tests

The probability of the 336 patients transplanted in first complete remission being alive at 3 years was 34%. The disease-free survival probability was 23%, and the relapse risk 68% (Table 2). Autologous BM HSCT was

Table 1. **Characteristics of 336 patients with myelodysplastic syndromes, secondary acute myeloid leukemia or therapy-related myelodysplasia/leukemia who received an autologous bone marrow (BM) or peripheral blood (PB) stem cell transplantation in first complete remission after 1992.**

	BM	*PB*	*p value*
Age (years)	104	232	< 0.001*
0-29	22 (21)	20 (9)	
30-39	20 (19)	29 (14)	
40-49	26 (25)	46 (20)	
50-59	28 (27)	77 (33)	
>60	8 (8)	60 (26)	
Transplant year			< 0.001*
1993-1996	60 (58)	55 (24)	
>1996	44 (32)	177 (76)	
Interval diagnosis-Transplantation (months)			< 0.04*
< 5	28 (27)	78 (34)	
5-8	43 (41)	105 (46)	
≥ 8	33 (32)	47 (20)	
Disease classification			< 0.15°
Primary MDS	24 (23)	41 (17)	
Secondary acute leukemias	30 (29)	62 (27)	
Therapy-related MDS/AML	21 (20)	35 (15)	
MDS unknown history	29 (28)	94 (41)	
Cytogenetics (Greenberg) N=136			< 0.11°
Standard	26 (62)	33 (56)	
Intermediate	15 (36)	18 (31)	
High	1 (2)	8 (13)	

**χ^2 test for linear-by-linear association (trend test); °χ^2 test for association.*

performed in 104 patients and 232 patients received autologous PB stem cells. The 3-year disease-free survival was slightly better after BM than after PB (28% and 21%, respectively) because of an apparently higher relapse risk (p=0.07) in the recipients of mobilized PB stem cells. However, the mean age of BM recipients was significantly younger (41 years±15 years) than that of the PB recipients (50 years±14 years). Age had a significant impact on the 3-year relapse rate and treatment-related mortality of the 336 patients autografted in first complete remission (Table 3). This translated into a trend (p=0.12) to a lower disease-free survival in the older age groups (Table 3). After correction for confounding factors, such as age, the relapse risk after autologous PB HSCT was not higher than that after BM HSCT.

The disease-free survival of patients with therapy-related MDS/AML was significantly better than that of the other patients (Table 2). This difference cannot be explained by a different age distribution in the various disease categories since the age distribution was not significantly different (*data not shown*). The use of BM and PB stem cells was similar in all disease categories (*data not shown*). The interval between diagnosis and transplantation did not influence the outcome significantly. Transplantations performed after 1996 resulted in significantly lower disease-free survival (20%) compared to 29% in the earlier period, mainly due to a higher patient age in the more recent cohort (*data not shown*).

Table 2. **Three-year disease-free survival (DFS), relapse rate, and transplant-related mortality (TRM) of 336 patients transplanted in first complete remission with either autologous bone marrow or mobilized blood stem cells (univariate calculations).**

	Number	*DFS#*	*Relapse$*	*TRM$*
All patients	336	24	61	13
BM HSCT	104	28	56	12
PB HSCT	232	21	64	13
p value		0.22	0.07	0.99
Age				
0-29	42	24	57	11
30-39	49	30	53	13
40-49	72	29	64	3
50-59	105	18	66	16
>60	68	16	66	18
p value		0.12	0.02	0.05
Type of MDS				
Acute leukemia after MDS	92	15	70	13
Primary MDS	65	24	65	6
Therapy-related MDS	56	48	39	12
Unknown	123	14	67	17
p value		0.002	0.005	0.34
Cytogenetics (Greenberg)				
Standard	59	31	50	12
Intermediate	33	41	46	9
High	9	56	44	0
Unknown	235	16	69	14
p value		0.32	0.88	0.57
Interval diagnosis-transplantation				
≤ 5 months	107	24	63	11
5-8 months	147	27	59	12
> 8 months	80	17	62	15
p value		0.28	0.31	0.56
Transplant year				
1993-1996	115	29	57	11
>1996	221	20	63	14
p value		0.04	0.09	0.41

#DFS estimated by the Kaplan-Meier method; $TRM and relapse estimated as cumulative incidences in a competing risk model; p values: log-rank test (likelihood-ratio test) from a univariate Cox model. The trend version of the log-rank test is used when two or more ordered categories are involved.

Multivariate analyses (Cox Model)

The main aim of the multivariate Cox model was to test the value of transplantation with mobilized PB stem cells on the various outcomes. This analysis compared the outcome of autologous PB versus BM HSCT after having adjusted for age, transplant year, interval diagnosis - transplantation and stage/type of MDS at transplantation (primary MDS, AML-MDS vs. therapy-related MDS/AML-MDS). Therefore, the interactions of autologous PB HSCT with all other covariates were tested in a stepwise backward manner. The disease-free survival was not different after PB or BM transplantation with a hazard ratio (HR) of 0.92 and a 95% confidence interval (CI) of 0.67 - 1.30 (p=0.65). The relapse risk after both forms of autologous HSCT was also almost identical with a HR of 1.1 (Table 3). An interval between diagnosis and transplantation of more than 6 months tended to be associated with a better disease-free survival rate and a significantly lower relapse risk (Table 4). Age had no impact on disease-free survival when adjusted for the other variables, but there was a trend (p=0.2) towards a higher relapse risk in the older

Table 3. Multivariate analysis for disease-free survival (DFS) and relapse with main effects only.

Risk factors for DFS	*Categories compared*	*Hazard ratio*	*95% Confidence interval*		*p value*
			Lower	*Upper*	
Source of stem cells	PB	(1)	0.7	1.3	0.66
	BM	0.9			
Interval diagnosis transplantation	<6 months	(1)	0.7	1.0	0.08
	≥6 months	0.8			
Age	10 year cohorts	1.0	0.9	1.1	0.66
Calendar year	Continuous variable	1.1	1.0	1.2	0.03
Disease categories	AL after MDS	(1)			
	Primary MDS	0.9	0.6	1.3	
	Therapy-related MDS	0.4	0.3	0.7	0.004
	MDS with unknown history	0.9	0.6	1.2	
Risk factors for relapse	*Categories compared*	*Hazard ratio*	*95% Confidence interval*		*p value*
		Lower	*Upper*		
Source of stem cells	PB	(1)			0.47
	BM	1.2	0.8	1.7	
Interval diagnosis transplantation	<6 months	(1)			0.04
	≥6 months	0.8	0.6	1.0	
Age	10 year cohorts	1.1	1.0	1.2	0.19
Calendar year	Continuous variable	1.0	0.9	1.1	0.63
Disease categories	AL after MDS	(1)			
	Primary MDS	0.8	0.5	1.3	
	Therapy-related MDS	0.4	0.3	0.7	0.007
	MDS with unknown history	1.0	0.7	1.5	

PB: peripheral blood; BM: bone marrow.

age cohorts (Table 3). Calendar year had an adverse effect: the HR was around 1.1 (95% CI 1.0-1.2; p=0.03) denoting an increase in the event rate of 10% per calendar year. Patients with therapy-related MDS/AML may expect a significantly better event-free survival after autologous HSCT compared to patients with other forms of disease, even after adjustment for confounding factors in the Cox model, including interval between diagnosis and transplantation (Table 3).

Comparison of autologous BM and PB stem cell transplantation in various age groups

We observed an age-dependent difference in outcome in earlier comparisons of autologous BM versus PB HSCT. Therefore we compared the results of the two types of HSCT in the various age groups adjusted for confounding factors such as transplant year, disease category, and interval between diagnosis and transplantation. A significant interaction (p=0.02) between age and the source of stem cells was detected in this analysis (Table 4). The HR for disease-free survival between PB and BM recipients was significantly lower in the younger age groups than in the older age groups denoting a favorable potential of autologous PB stem cell transplantation in young age groups. This interaction can be explained by a significantly lower transplant-related mortality of PB HSCT carried out at a lower age when compared with BM HSCT (p=0.04). The same was true for the relapse risk but this interaction was not statistically significant (p=0.29). Table 4 shows the estimated hazard ratios and confidence intervals in the various age groups.

Table 4. Results of a multivariate Cox analysis for disease-free survival (DFS) relapse and treatment-related mortality (TRM). Comparison of PB versus BM in various age groups, adjusted for the interval between diagnosis and transplantation, disease categories, and transplant year including significant interactions.

Outcome	*DFS*				*REL*				*TRM*			
Age (yrs)	*HR*	*95% CI*		*p value*	*HR*	*95% CI*		*p value*	*HR*	*95% CI*		*p value*
		lower	*upper*			*lower*	*upper*			*lower*	*upper*	
20	0.5	0.2	0.9	0.02	0.8	0.3	1.8	0.5	0.1	0.02	0.8	0.03
40	0.8	0.6	1.1	0.20	1.1	0.7	1.6	0.8	0.4	0.2	1.0	0.07
60	1.4	0.8	2.3	0.19	1.4	0.8	2.6	0.2	1.5	0.5	4.3	0.5

*Disease-free survival: interaction PB/BM *Age: HR=1.3 (95% CI = [1.05-1.7], p=0.02; the HR of PB versus BM increases by a factor of 1.3 for every 10 years of patients' age. Relapse: interaction PB/BM *Age: HR=1.2 (95% CI = [0.9-1.6], p=0.29; the HR of PB versus BM increases by a factor of 1.2 for every 10 years of patients' age. Transplant-related mortality: interaction PB/BM *Age: HR=1.9 (95% CI=[1.0-3.4], p=0.04; the HR of PB versus BM increases by a factor of 1.9 for every 10 years of patients' age. Model: source of stem cells, year, interval diagnosis-transplantation, disease type, source. *Age, Year *Age.*

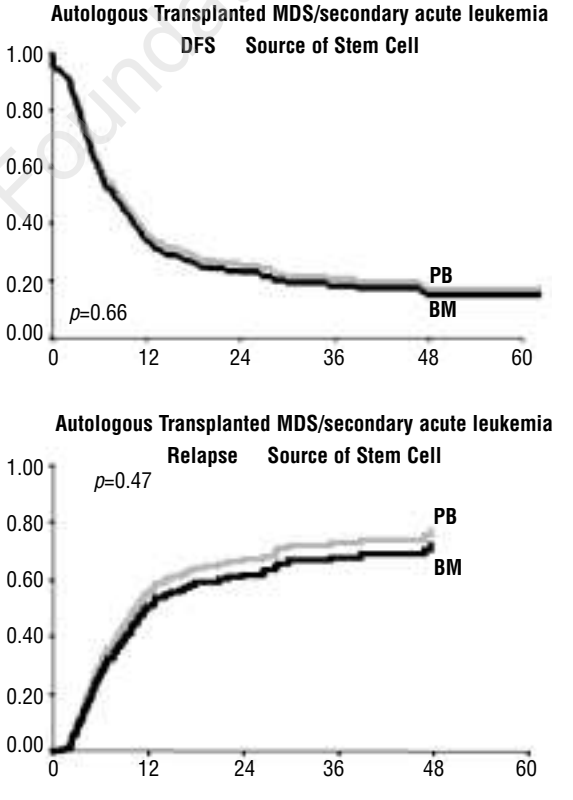

Figure 1. Cox model to compare the impact of autologous PB versus BM HSCT on disease-free survival (DFS) (upper panel) and relapse risk (lower panel) after adjustment for age, calendar year, interval diagnosis-transplantation, disease. Hazard ratio (PB vs BM) for DFS: 0.9 (p=0.66). Hazard Ratio (PB vs BM) for relapse: 1.2 (p=0.47).

Discussion

The experience with autologous transplantation in high-risk MDS is limited.[17-19,22] The EBMT reported a 3-year survival of 38% for patients transplanted in first complete remission.[22] A French co-operative group study reported on autologous stem cell transplantation in 83 patients with MDS.[22] Transplantation was performed in 24 of the 39 patients (62%), who achieved complete remission. The median overall survival was 33 months from transplantation. The hematopoietic recovery after autologous BM stem cell transplantation for myeloid malignancies is generally slow. Administration of a high number of stem cells, obtained by mobilization of the stem cells into the peripheral blood, may improve the speed of engraftment. Pilot studies showed the feasibility of collecting peripheral blood stem cells from patients in complete remission of MDS.[23,24] In a study in 11 patients in complete remission after chemotherapy, stem cell mobilization was attempted either with granulocyte colony-stimulating factor (G-CSF) alone or with G-CSF after recovery from the consolidation course. In seven of these 11 patients sufficient numbers of cells were harvested, resulting in a CD34 progenitor cell yield >1×10^6/kg.[24] Carella *et al*. were able to collect normal progenitor cells from six out of nine patients who presented with an abnormal karyotype.[24] In our own experience stem cell mobilization was feasible in about 50% of patients in the recovery phase after chemotherapy with G-CSF.[25]

Since MDS are clonal hematopoietic stem cell disorders, there remains concern regarding contamination of the graft by residual malignant cells, especially if high numbers of mobilized stem cells are used for autologous HSCT. Several studies have reported that patients with an abnormal karytotype can achieve a cytogenetic remission if a morphological remission is reached after chemotherapy. Delforge *et al*. reported that polyclonal immature hematopoietic progenitors can be mobilized and harvested in patients with high-risk MDS after treatment with intensive chemotherapy.[26] Clonality analysis was performed in females heterozygous for the X-linked human androgen-receptor (HUMARA) gene demonstrating a polyclonal pattern in the $CD34^+$ cell population in four out of five patients. Murine models in which no clonal (cytogenetically aberrant) precursors were identified in NOD/SCID mice transplanted with marrow from patients with MDS more than 2 months after transplantation[27] support the polyclonal normal nature of MDS marrow in complete remission after intensive antileukemic treatment.

The present analysis was performed to assess the value of autologous PB stem cell transplantation in the treatment of patients with high-risk MDS. Ideally, this question should be studied in a prospective setting, but the number of patients eligible for this treatment approach is too low to perform such a study within a reasonable period. Therefore, we performed retrospective analyses on the data from the EBMT registries to assess the role of autologous PB HSCT in patients with MDS. We were confronted with two major confounding factors: a substantial age increase in more recently performed autotransplantations and a poorer outcome of autologous BM HSCT recipients whose transplant was performed before 1992. Therefore we restricted the analyses to transplants performed after 1992. In addition we adjusted the outcome for age and other potentially confounding factors. The 3-year disease-free survival of the 336 patients transplanted in first complete remission was 24%. The relapse risk of 68% accounted for the main cause of failure. The 3-year disease-free survival was slightly better after BM than after PB HSCT (28% and 21%, respectively), but the mean age of BM recipients was significantly younger (41 years±15 years) than that of PB recipients (50 years±14 years). The higher average age may have contributed to the higher transplant-related mortality and relapse rate after PB HSCT. The multivariate Cox model adjusted the outcome of PB versus BM HSCT for age, transplant year, interval between diagnosis and transplantation and stage/type of MDS at transplantation (primary MDS, AML-MDS vs. therapy-related MDS/AML-MDS). The adjusted disease-free survival and relapse rates were not different after transplant using the two stem cell sources. Age had no impact on disease-free survival when adjusted for the other variables, but there was a trend (p=0.2) towards a higher risk of relapse in the older age cohorts probably due to other age-related factors such as adverse cytogenetic characteristics. When the impact of age on the two forms of HSCT was analyzed separately, it appeared that the outcome after PB HSCT was significantly better in patients younger than 30 years in contrast to the equivalent outcome in older age groups. The explanation is speculative, but the higher incidence of adverse cytogenetic characteristics usually observed in older MDS patients may have contributed to this effect. In addition, the transplant-related mortality rate after PB HSCT was significantly lower in the young age groups, probably reflecting a more rapid hematopoietic recovery after PB stem cell transplantation in these young patients. A confusing outcome was the adverse effect of calendar year. The HR was around 1.1 (p=0.03) denoting an increase in event rate of 10% per calendar year. However, the mean follow-up time (among patients still alive) is decreasing steeply and more than to be expected from 1995 onwards. This may indicate a selection bias due to mortality overreporting of recently transplanted patients.

Patients with therapy-related MDS/AML had a significantly better disease-free survival than did those with the other categories of disease, even after adjustment for confounding factors in the Cox model, including interval between diagnosis and transplantation. The explanation of this unexpected outcome is not straightforward, but the contribution of patients with favorable cytogenetic characteristics might be relevant. We identified eight patients with t(8;21) or inversion 16 in an incomplete and ongoing analysis. The 3-year disease-free survival of these patients was 57% (*personal communication N. Kröger*).

Reports in the literature suggest that allogeneic stem cell transplantation is superior to autologous transplantation, producing disease-free survival rates varying from 35-45%.[4-9,11,28,29] However all these studies have reported

observational data. Selection of patients fit enough to go through an allogeneic stem cell transplantation procedure may introduce a selection bias. A multicenter study by the EORTC, EBMT, the Swiss Group for Clinical Cancer Research (SAKK) and Gruppo Italiano Malatie Ematologiche dell'Adulto (GIMEMA) compared the results of 159 patients who received remission-induction chemotherapy and were then candidates for allogeneic and autologous stem cell transplantation depending on the availability of an HLA-identical sibling.[30,31] The percentage of patients who received the intended allogeneic transplantation (69%) was significantly higher than the percentage who underwent autologous transplantation (49%) ($p<0.05$), as observed for patients with AML.[32,33] The 4-year event-free survival was 23% for patients with a donor and 22% for patients without a donor ($p=0.66$). The results of this EORTC study[22] suggest that patients with high-risk MDS and AML-MDS may benefit from either allogeneic or autologous SCT.

The results of this study (EORTC 06921) were compared with those of 215 MDS and AML-MDS patients treated at the MD Anderson Cancer Center.[34] The 215 patients in the American study had received various high-dose cytarabine-containing induction regimens, and after remission-induction continued to receive these regimens at reduced dosage for 6-12 months. Remission rates were 54% and 63%, respectively ($p=0.09$). Sixty-five of the EORTC patients who entered complete remission received a transplant during the first remission. Disease-free survival in patients achieving complete remission was superior in the EORTC cohort, the 4-year rates being 29% in the EORTC cohort versus 17% in the M.D. Anderson group ($p=0.02$), but survival in the two groups was not significantly different.

A substantial number of patients may not reach the autologous stem cell transplant procedure because of failure to achieve remission or failure to produce sufficient numbers of stem cells. Careful clinical evaluation of the prognostic factors, such as age, cytogenetic characteristics, chance of achieving complete remission, and availability of a matched unrelated donor should guide the treating physician in advising the patient about the available treatment options. The option of autologous PB stem cell transplantation may be considered a reasonable alternative for patients lacking a donor. Mobilized PB stem cells are the preferred stem cell source for young patients, especially in view of the more rapid hematopoietic recovery after transplantation with such stem cells, but BM stem cells may also be considered for patients over 50 years old. Further development of precise prognostic classification systems, including an accurate cytogenetic/molecular response evaluation to chemotherapy, is needed to develop a risk-adapted strategy for individual patients.

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